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Date of Signature and Deposit: 2/8/05

Jean C. Baker

Jean C. Baker, Reg. No. 35,433

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Hector F. DeLuca, et al.
Serial No.:	09/769,579
Filed:	January 25, 2001
For:	METHOD OF TREATMENT OF TYPE I DIABETES
Group Art Unit:	1617
Examiner:	S. Sharareh

Commissioner For Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF JULIA ZELLA

Dear Sir:

1. I, Julia Zella, am one of the named inventors in the above-identified patent application and a Research Associate in the Department of Biochemistry, University of Wisconsin-Madison. I have reviewed the September 9, 2004 Office Action in the above-identified case and two references cited by the Examiner during the prosecution of the above-identified case: Mathieu, et al. Diabetologia, 1994 and Mathieu, US Patent 5,665,387. I do not believe that the method of the present invention is anticipated by either reference because neither reference demonstrates reduction of diabetes symptoms by $1,25(OH)_2D_3$.

2. When Professor Hector DeLuca and I began studying the effect of vitamin D compounds in diabetes in 2000, we attempted to replicate the work disclosed in Mathieu, Diabetologia, 1994. I was unable to replicate the result.

Attached you will find the diabetes incidence graph for the "injection study" I performed (Exhibit A). Comments about this study as follows:

a. I received and reviewed the pertinent sections of Mathieu, et al. U.S. '387. The method I designed to treat the animals was meant to replicate Mathieu, et al., Diabetologia, 1994 and agrees with that described in U.S. Patent '387, column 5 of the text, with the following exceptions:

i. Diet: U.S. Patent '387 used 0.2% calcium, 1% P diet + D; we used 0.47% calcium, 0.3% P + D (Diet 11).

ii. Vitamin D compound: U.S. Patent '387 states that the $1,25(OH)_2D_3$ was dissolved in arachis oil and vehicle treated animals received arachis oil only. Our $1,25(OH)_2D_3$ was in EtOH, then dissolved in arachis oil (<5% v/v).

iii. Diabetes determination: Mathieu used replicate serum glucose measurements to determine diabetes; I used a combination of a positive urine test and a duplicate serum glucose measurement.

I believe these differences to be trivial and to have no effect on experimental outcome.

3. The outcome of my experiments reported in Exhibit A are as follows:

a. Serum calcium: U.S. Patent '387 terminal serum calcium values reported as (2.2 ± 0.2) mmol for vehicle and (2.5 ± 0.2) mmol for 1,25-treated mice. At 70 days of age (when glucose monitoring began), our vehicle and 1,25-treated mice had serum calcium values of (8.9 ± 0.5) mg/dL and (10.3 ± 0.4) mg/dL, respectively. The serum calcium levels, although expressed in different units, are similar. Therefore, the serum calcium responses to the treatments for both labs seem to agree.

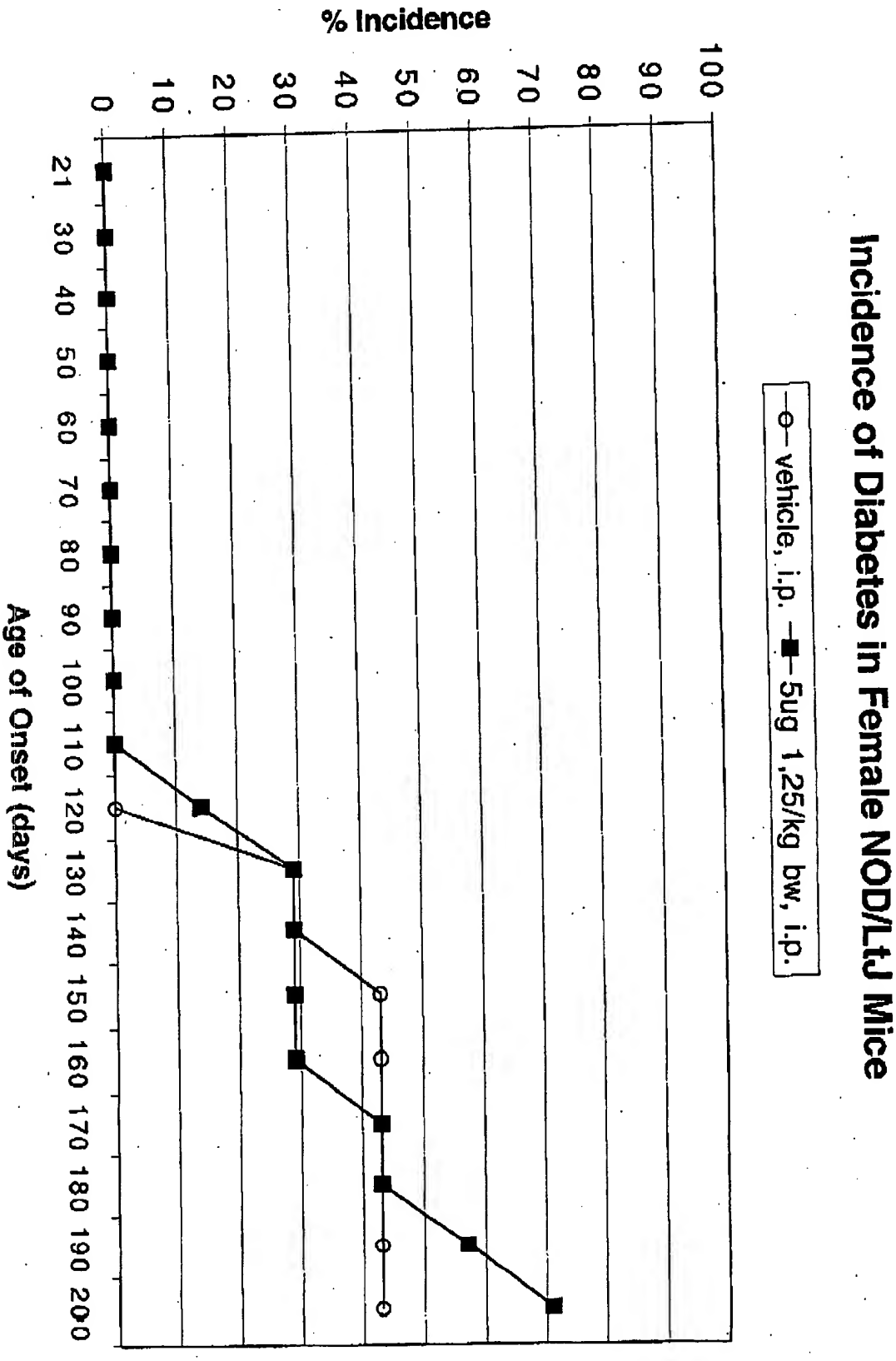
b. Statistics: Both Mathieu, et al. documents demonstrate a reduction in diabetes incidence from 56% (N=40) to 8% (N=40) in mice treated with 1,25. Using the Fisher exact test, I confirmed this is statistically significant ($P<0.001$). Our data show a diabetes incidence that is not decreased by 1,25-injection (43% and 71%, respectively). We had 7 animals per treatment group and, using the same statistical test, our data are not statistically significantly different between groups ($p>0.5$).

3. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the above-identified application or any patent issuing thereon.

Respectfully submitted,

Date: 02.07.05

Julia Zella



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